REMARKS

Claims 1-36 are now pending in the application (claims 21-36 having been added by the present amendment).

Claims 1, 4-9, 10-13, and 15-16 have been amended. **Claim 1** has been amended to specify that "within the HBV core antigen, at least one and not more than 25 of the amino acid residues are substituted.", and at least one amino acid substitution." Support for this amendment can be found, for example, at page 3, lines 12-16. **Claim 4** has been amended to recite a "mycobacterial" stress protein. Support for this amendment can be found, for example, at page 4, lines 12-15. **Claim 5** has been amended to depend from claim 4 and to limit the mycobacterial stress protein to an *M. bovis* BCG stress protein, and **claim 6** has been amended to depend from claim 5 and to limit the *M. bovis* BCG stress protein to an *M. bovis* BCG hsp65 stress protein. These amendment is supported by, for example, original claim 4 and the specification at page 10 (*see also*, Example 1). **Claims 10 and 16** have been amended to correct minor or grammatical errors. **Claims 7 and 11** have been amended to reference SEQ ID Nos. (rather than Figures), and **claims 8, 10, 12, 13, 15, and 16** have been amended in their dependencies.

New **claims 21-23** further limit the number of amino acid residues within the HBV core antigen that can be substituted. Support for these claims can be found in the specfication at, for example, page 3, lines 12-16. New **claim 24** specifies that "at least one of the substitutions generates a mouse MHC-restricted CTL epitope within the HBV core antigen." Support for this claim can be found in the specfication at, for example, page 7, lines 21-24. New **claims 25-33** depend, or ultimately depend, from claim 24, and further limit the substitutions made within the HBV core antigen. These claims are supported by the specification at, for example, page 7, lines 24-31; page 8, lines 20-30; and page 19, lines 7-9. New **claims 34-36** are supported by original claims 12, 14, and 13, respectively. No new matter has been added.

35 U.S.C. § 112, ¶ 2

Claims 7-20 are rejected as being indefinite because claims 7 and 11 (from which claims 8-10 and 12-20, respectively, depend) refer "to a figure instead of a SEQ ID number" (Office action at page 2). In response, Applicants have amended claims 7 and 11 to refer to SEQ ID numbers, rather than figures. This ground for rejection can therefore be withdrawn.

Claim Objections

Claims 12-15 were objected to under 37 CFR 1.75(c) as being in improper form (Office action at page 2). In response, Applicants have amended claims 12, 13, and 15 to correct their dependencies. As claim 14 depends from claim 12, which is now in proper form, claim 14 is also now in proper form. Applicants' representative apologizes for the errors.

35 U.S.C. § 103

Claims 1-4, 8-10, 12, and 14-18 are rejected as being obvious over U.S. Patent No. 6,338,963 (herein, "Young") in view of U.S. Patent No. 4,547,368 (herein, "Tabor"). For the sake of completeness and easy reference, the Examiner's argument is reproduced here in its entirety (Office action at page 3):

> Young teaches broadly that fusion of a stress protein to an antigen induces or enhances an immune response against the antigen. Young teaches a viral antigen as appropriate, see for example claim 6, 24, 43, 51, 75. This differs from the claimed invention in that Young does not specifically teach hepatitis B virus [HBV] core antigen. However, Tabor teaches HBV core antigen as a desirable immunogen. Therefore it would have been obvious to choose this species of virus antigen for use as broadly taught by Young, with reasonable expectation of success.

In view of the present amendment, Applicants respectfully request reconsideration and withdrawal of this ground for rejection. Claim 1 has been amended to limit the HBV core antigen to one in which "at least one and not more than 25 of the amino acid residues are substituted." Neither Young nor Tabor in any way suggests such a modified HBV core antigen. Indeed, as the Examiner noted, "Young does not specifically teach hepatitis B virus core

antigen" at all. As the prior art must teach or suggest all the limitations of the claim (MPEP at 2142), and as that requirement cannot be met with respect to amended claim 1, there is no *prima facie* case of obviousness.

Claims 5 and 6 are rejected as being obvious over Young and Tabor (as applied to the claims discussed above) and further in view of U.S. Patent No. 6,231,864 (herein, "Birkett"). The Examiner states that claims 5 and 6 (Office action at pages 3-4):

> differ from the above [the fusion protein discussed above] in that they (*sic.*) require removal of all or a part of the C-terminal arginine-rich domain of HBV core antigen. Birkett teaches that this region is undesirable because it binds DNA [citations omitted]. Terefore it would have been obvious to remove this region to avoid this complication, with reasonable expectation of success.

In view of the present amendment of claims 4-6, this ground for rejection should be withdrawn. Claims 5 and 6 have been amended to cover specific stress proteins; they no longer limit the HBV core antigen in any way, let alone a way suggested by Birkett (Applicants wished to disturb the claim numbering as little as possible). Accordingly, this ground for rejection should now be withdrawn.

Claims 19 and 20 are rejected as being unpatentable over Young in view of Tabor and further in view of Mizzen *et al.* (WO 98/23735; herein, "Mizzen"). The Examiner states that claims 19 and 20 (Office action at page 4):

> differ from the above [claims] by requiring administration of a nucleic acid encoding the fusion protein. Mizzen teaches that the nucleic acid is an alternative to the protein for in vivo administration of a stress protein/antigen fusion [citations omitted]. Therefore it would have been obvious to use this alternative immunization method, with reasonable expectation of success.

In view of the present amendment of claim 1, from which claims 19 and 20 ultimately depend, this ground for rejection should be withdrawn. Claim 1 now covers a fusion protein that includes an HBV core antigen that contains at least one, but not more than 25, amino acid substitutions. Neither Young nor Tabor, alone or in combination, suggest such a fusion protein. Nor does Mizzen suggest a nucleic acid that encodes it. As the prior art does not teach or suggest all the limitations of the present claims, there is no *prima facie* case of obviousness.

Lastly, claims 10, 12-15, 19, and 20 are rejected as being unpatentable over either U.S. Patent No. 6,020,167 (herein, "Thoma") or U.S. Patent No. 6,297,048 (herein, "Jolly") in combination with Young. The Examiner states (Office action at page 4):

> Both Thoma and Jolly teach a retroviral vector expressing HBV core antigen, and its therapeutic use. This differs from the invention in that neither reference teaches fusion of the antigen to a stress protein. However, Young teaches improved immune response to any antigen fused to a stress protein, and improved immune response is always desirable. It would have been within the ordinary skill of the art to modify Thoma or Jolly by fusing a stress protein (or portion thereof) to the HBV core antigen sequence, for the purpose of improving the immune response, with reasonable expectation of success.

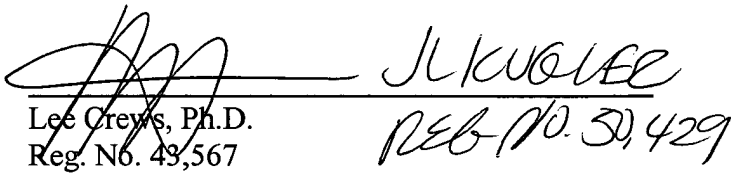
Here again, in view of the present amendment, Applicants respectfully request reconsideration and withdrawal of the rejection. All of claims 10, 12-15, 19, and 20 ultimately depend from claim 1, which requires a fusion protein that contains an HBV core antigen in which at least one, but not more than 25, of the amino acid residues have been substituted. Thoma does not suggest such a modified HBV core antigen. Neither does Jolly. Accordingly, neither of these references, even in combination with Young, can suggest a nucleic acid (as covered by Applicants' claim 10) or a vector (as covered by Applicants' claims 12 and 13), or any other composition or method that requires an HBV core antigen modified as Applicants claims now require. As it is well established that the prior art cannot render a claimed invention obvious unless it teaches or suggests all the limitations of the claims, and as there is no teaching or suggestion in the prior art of an HBV core antigen that includes at least one, but not more than 25, substituted amino acid residues, there can be no *prima facie* case of obviousness. The rejection should, therefore, be withdrawn.

CONCLUSION

In view of the foregoing, Applicants contend that the present claims are now in condition for allowance, which action is respectfully requested. Filed herewith is a Petition for Extension Time, and the requisite fee. If there are any other charges, or any credits, please apply them to Deposit Account No. 06-1050, referencing Attorney Docket No. 12071-017002.

Respectfully submitted,

Date: November 20, 2003



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